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Formulation of Nasal Gels of Vitamin B12-I Effect of Additives on Thermodynamic Properties of Pluronic PF-127 Gels

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Short nasal residence, a major limitation of nasal route can be overcome by gel formulation. Therefore, an attempt has been made to formulate thermoreversible nasal gel of vitamin B12 which is poorly absorbed through oral route. Pluronic (PF127) was selected as a gelling agent and effect of polymer concentration, presence of drug, osmolarity agent and gel point enhancer PEG 15000 (PEG) on thermodynamic properties of the gels is discussed in this work.

Accurately weighed quantity of PF 127 was hydrated with aqueous phase containing suitable quantities of drug and additives. The mixture was stored at - 4° for 12 h. Polymer concentration was 20%, 22% and 24 % w/w, vitB12 (0.52% w/w including overages), sorbitol 0.5 M, 1.0 M and 1.5 M and PEG 0.6%, 1.1% and 1.6 %w/w. For determination of gelation temperature (T1) and gel melting (T2), a sealed test tube containing 2 ml gel was equilibrated at 4° and temperature was increased at the increment of 1°. T1 was recorded when meniscus does not move on tilting at 900 and T2 , when gel starts flowing.

For plain gels T1 decreases and T2 increases with PF127 concentration. Gelation range broadens in presence of vit.B12 whereas sorbitol narrows it due to greater suppression of T2 as compared to T1.The enthalpy of gelation (DHogel) and enthalpy of melting (DHomelt) of the polymer were determined using Eq.1 and Eq 2 , where C is polymer conc. The extent of suppression of T2 is significantly higher as compared to T1. The DHogel and DHomelt were 6.066 and _ 3.097 Kcal/ mole resp.
3.097 Kcal/ mole resp. ln C = DHogel / RT1 + constant — Eq. 1 ln C = DHomelt/ RT2 +constant — Eq. 2 In presence of sorbitol a linear relation was observed in the semilogarithmic plot of PF127 concentration and reciprocal of gel melting temperature. The DHogel for sorbitol concentrations 0.5 M, 1 M and 1.5 M were -4.049, -1.795 and _0.28 Kcal/mole respectively. Similarly linearity was observed for T2 at different concentrations of PEG (-2.014 to 2.714 Kcal/mole). Gelation occurs due to progressive dehydration of polymeric micelles. The high water solubility of vit B12 favors the salting out of polymer. At gel melting vit B12 favors the hydration of the PEO chains of polymer and thus increases T2. The drug molecule does not alter the enthalpy, suggesting no interaction with the polymer. Sorbitol decreases T1 and DHogel due to formation of H-bonds with etheral oxygen of polymer and formation of crosslinks with lower DHo. Difference in T2 reduces and DHomelt increases with sorbitol. PEG forms mixed micelles Thermodynamic properties of PF127 gels are dependent on concentration of polymer and water soluble materials. The gelation range narrows in presence of sorbitol and PEG. The enthalpy change was significant in gels containing sorbitol

and PEG.

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